EDITORIAL
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AXILLARY SURGERY IN BREAST CANCER: ARE WE NEAR THE END OF THE ROAD

Cirurgia axilar no câncer de mama: estamos próximos ao fim da estrada?

Cleverton César Spautz[1]*

Surgical treatment of breast cancer has always addressed the breast and axilla together, and it was restricted until some decades ago to radical mastectomy. The first major change in breast approach occurred in the 1980s when Veronesi and Fischer introduced conservative breast surgery along with radiotherapy while maintaining axillary dissection[1,2].

The possibility of more conservative surgical treatments culminated in breaking the paradigm that linked success to surgical radicality. With a better understanding of the natural history of the disease, there were changes in treatment that included chemotherapy, radiotherapy and hormone therapy, and even more recent lines such as target therapy and immunotherapy. The use of multiple therapeutic fronts propelled the search for less aggressive surgical treatments.

Despite the evolution of surgical techniques in the approach of the breast, axillary dissection was maintained. However, it is known that the consequences of this procedure, from the functional point of view, are more severe than the mastectomy itself. Lymphedema and monoparesis are frequent complications in this surgery, often progressive and irreversible, leading to substantial limitations in the daily lives of patients.

Because of the concern about reducing axillary dissection morbidity, in the late 1990s, the sentinel lymph node technique emerged, which allows patients with negative lymph nodes to be spared from axillary dissection.[3]

In the following years, the sentinel lymph node technique was established as the most appropriate for patients with a clinically negative axilla, leaving axillary dissection restricted to cases in which there was lymph node involvement. However, despite the continuous increase in early diagnosis linked to extensive screening campaigns, a still significant proportion of women with breast cancer have lymph node involvement at diagnosis. This is due to two factors: delayed diagnosis due to screening failure and aggressive tumor behavior itself.

After more than 10 years of using the sentinel lymph node procedure, a new step has been taken towards lower morbidity. Giuliano et al. led the American College of Surgeons Oncology Group Z0011 (ACOSOG Z0011) study, which demonstrated that even women with low lymph node involvement (1-2 lymph nodes without extracapsular spread) can avoid axillary dissection without increased risk of recurrence.[4] Interestingly, when the axillary dissection group was analyzed, 27.3% of the women had other involved lymph nodes, in addition to the sentinel lymph node(s), without survival impairment, which demonstrates the effectiveness of the adjuvant treatments. These data were corroborated in 2017 in an update of the same study with a 9.3-year follow-up showing no difference between groups in overall survival, disease-free survival, and axillary recurrence.[5]

Also, as an alternative to axillary dissection, AMAROS, a non-inferiority study, compared axillary dissection with axillary radiotherapy and concluded that the latter was not inferior in terms of overall and disease-free survival with lower lymphedema rate in the radiotherapy group.[6]

With the use of neoadjuvant treatments came the new possibility of less aggressive surgical treatments. This was clear from the outset for the breast approach, which made it possible to use conservative surgery in women who had previously undergone mastectomy. However, in patients with positive lymph nodes prior to neoadjuvant therapy, the use of sentinel lymph nodes is still debatable. Important points include lower lymph node identification rate as well as higher false-negative rate.

Questions arose: when is the ideal time to do the sentinel lymph node procedure, before or after neoadjuvants? What is the appropriate method, using one or two tracers? And what is the optimal number of resected sentinel lymph nodes? Further studies have been conducted in an attempt to answer these questions.

[1]Centro de Doenças Mama/Oncoclínica, Hospital Nossa Senhora das Graças – Curitiba (PR), Brazil.
***Corresponding author:** ccspautz@gmail.com
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In the Sentinel Neoadjuvant (SENTINA) study, women were divided according to axilla status: positive or negative. Those with a negative axilla underwent sentinel lymph node evaluation before chemotherapy with an identification rate of 99.1%. Those with clinically positive axilla underwent sentinel lymph node biopsy after neoadjuvant therapy with an identification rate of 80.1% and respective false-negative rates of 24.3 and 18.5% when one or two lymph nodes were removed. The change in lymphatic drainage pattern due to chemotherapy response explains this difference in identification rate and the high false-negative rate found.[7]

ACOSOG Z1071 evaluated only women with a biopsy-proven positive axilla who had undergone neoadjuvant chemotherapy. The identification rate was 92.7% and the use of two tracers for sentinel node identification was more effective than one. The false-negative rate was 12.6% with a clear relationship with the number of sentinel lymph nodes found. When three or more sentinel lymph nodes were identified, the false negative was 9.1%.[8,9]

The use of lymph node tracers at the time of biopsy made it possible to improve the reliability of the sentinel lymph node technique. As already mentioned, changes occur in the lymphatic drainage path after neoadjuvant treatment, which makes the identification of the correct lymph node impossible in 23% of cases.[10]. The advantage of prior marking of the axilla is the certainty that the involved lymph node is resected. Clips, radioactive iodine (I^{125}) seed and charcoal are the most commonly used materials for this purpose.

Marking the axilla with radioactive iodine seeds (MARI) to indicate involved lymph nodes demonstrated a 97% identification rate and a 7% false-negative rate, proving to be a suitable method.[11]

Lymph node clip placement at the time of biopsy, target axillary dissection (TAD) and surgical removal in conjunction with the conventional sentinel lymph node technique (patent blue and radiolabeled colloid) achieved a false-negative rate of 1.4%, providing the technique with reliability.[10] The need for pre-surgical marking of previously clipped lymph nodes is considered inconvenient.

The charcoal method for lymph node marking has also been shown to be effective, with high identification rates (96.9–100%)[12-15]. It is a simple technique with injection of 0.1 to 0.5 mL of charcoal suspension into the lymph node capsule at the same time as the biopsy. At the time of surgery, it is then located by staining, combining it with the conventional sentinel node technique.

Therefore, in neoadjuvant therapy, sentinel lymph node use is feasible for those patients whose axilla has become clinically negative after systemic therapy. For its reliability, the following guidelines should be observed: use of two tracers, identification of three or more lymph nodes[16] or prior lymph node marking at the time of biopsy (clip, radioactive iodine seed or charcoal) and its resection during the surgery.

As with early stages, there are current studies to prevent axillary dissection in women who continue to have positive lymph nodes after neoadjuvant therapy. These include Alliance A011202, which randomizes women after neoadjuvant chemotherapy with positive sentinel lymph node(s) for axillary dissection (levels I and II) or axillary radiotherapy. It is expected to end in 2024.

We will still see major changes in axillary surgery. There is a constant search for procedures with maximum effectiveness and minimum morbidity. In a few years, axillary dissection will probably not be a part of breast cancer treatment. However, the use of sentinel lymph nodes or even less aggressive and more precise techniques will remain within the scope of breast cancer treatment for some time to come.

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